Modulation of chemokine release in cardiac endothelial cells by low doses of ionizing radiation *

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Introduction

More and more evidence has been provided, that exposure of the heart to even low doses (0.5Gy) of ionizing radiation significantly increase the risk for cardiovascular disease and in consequence leads to increased mortality [1-4]. The term "cardiovascular disease" describes different types of pathologies which affect the cardiovascular systems (e.g. coronary heart disease, heart failure, etc.). Several processes are discussed to be involved, e.g. pericardial or myocardial fibrosis, accelerated atherosclerosis, etc. [4]. In this context the endothelial dysfunction plays an important role in promoting fibrotic and inflammatory processes after irradiation [5]. Endothelial dysfunction is mainly characterized by a loss of thrombo-resistence of the endothelium, which is accompanied by an increased expression of adhesion molecules and van-Willebrand factor [5]. However the cellular and molecular mechanisms underlying the disease progression are not completely understood. Our part in this project is the investigation of the modulation of cytokine release by EC of the cardiovascular system after irradiation with low doses of high- and low LET radiation, in collaboration with partner institutes within the Procardio project, namely: the Helmholtz centre Munich, Germany and the Health protection agency (HPA) Chilton, UK.

Materials and Methods

For irradiation experiments, primary cardiac microvascular endothelial cells (HCMEC) were obtained from Lonza. In a first experiment, the cells have been irradiated with γ-rays at Helmholtz centre Munich and with nickel ions (175keV/µm) at GSI facilities (Darmstadt, Germany). Supernatant was taken 4 and 24h after irradiation and stored at -80°C. Measurements of the cytokine concentration were performed with ELISA technique and multiplex bead arrays (both from eBiosciences).

Results and Conclusion

The results of the first experiment where monocultures of HCMEC have been irradiated with nickel ions are shown in Figure 1. Measurements of the concentration of more than 20 cytokines or chemokines (e.g. TNF-α, MCP-1, MIP-1, IL-1α, IL-6, IL-8 etc.) revealed a tendency for a increased release of 2 chemokines (MCP-1 and IL-8) 24h after exposure, already at a dose of 0.5Gy. The other factors that have been investigated remained unchanged or the changes were statistically not significant (data not shown). No significant changes have been detected for all cytokines and chemokines measured after γ-exposure (not shown).

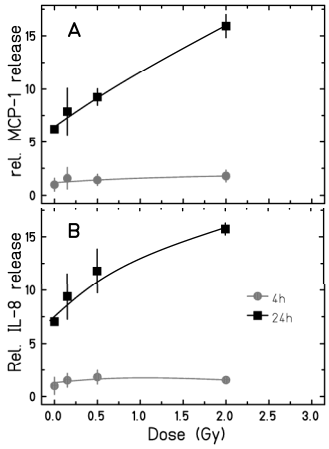

Figure 1: *Relative release of MCP-1 (**A**) or IL-8 (**B**) of HCMEC 4 and 24h after irradiation with nickel ions (LET: 175keV/µm).* (N=1, n=2)

The tendency for an increased release of the chemokines MCP-1 and IL-8 clearly points to an inflammatory reaction of HCMEC even after irradiation with low doses of ionizing radiation. The chemokine MCP-1 is mainly responsible to trigger monocyte recruitment into inflamed tissue [6], whereas IL-8 is responsible for recruitment of neutrophils and T-cells [7]. The higher amount of chemokines points to an increased migration of immune cells into the heart tissue after exposure to ionizing radiation, which than in turn could promote inflammatory processes like fibrosis or endothelial dysfunction. In future experiments the release of chemokines will be assessed more in detail, to clarify if the effect is statistically significant. As a next step the question will be addressed if a co-cultivation with other relevant cell types influences the responding cytokine/chemokine release.

References

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